

**REMARKS**

Claims 1-16 are pending in this application. Applicant respectfully requests reconsideration of the rejections, which are discussed below.

**Rejections of Claims 1, 3, 4, 16 under 35 U.S.C. § 102(a)**

The Office newly rejected claims 1, 3, 4, and 16 as being anticipated by Taketoshi et al (JP 2001-278810-A). The Office cites the following disclosures from Taketoshi:

- A composition hybrid of a drug with a layered silicate, pg. 13 [0004]
- Montmorillonite, pg. 13 [0004]
- a poorly water-soluble drug, pg. 13, [0004]
- cyclosporine, pg. 10, line 5
- layered silicates mixed with water, pg. 8, line 17; pg. 16, line 1
- amorphous character of composition, pg. 16, line 10
- increased solubility of the poorly water-soluble drug from adding the layered silicate to the drug, pg. 13, [0004]

Applicant respectfully disagrees.

The Office's rejection seems to be based on the presumption that since the layered silicates are mixed with water in Taketoshi, hydrogen ions from the water would form ionic bonds between the layered silicates and the drug. The examiner's presumption, however, is thermodynamically impossible. The hydrogen ions that can be released from water under room temperature, *i.e.*,  $1 \times 10^{-7}$ , would be too low to be substituted with interlayer cations. Rather, under such a low level of hydrogen ions, interlayer cations are hydrated by water molecules to stabilize the interlayer cations.

Applicant's theoretical explanation will be further supported by the Rule 132 Declaration, which will be subsequently submitted. The Rule 132 Declaration will show that the composition produced by the method disclosed in Taketoshi does not contain ionic bonds. More specifically, the test results will show that the Xray diffraction pattern

of the composition produced by the Taketoshi method is the same as that of the clay which does not contain ionic bonds. These test results, thus, will verify Applicant's explanation that the Taketoshi composition does not contain ionic bonds. Therefore, Taketoshi cannot anticipate the claimed hybrid wherein ionic bonds are formed between interlayer cations of the layered silicates and the drug. Accordingly, reconsideration and withdrawal of the anticipation rejection are respectfully requested.

**Rejections of Claims 1-16 under 35 U.S.C. § 103(a)**

The Office maintains the rejection of claims 1-16 under 35 U.S.C. § 103(a) as being obvious over Taketoshi et al in view of Jung et al (*Enhanced solubility and dissolution rate of itraconazole by a solid dispersion technique*. Int J Pharm. 1999 Oct 5; 187(2):209-18.) Applicant respectfully disagrees.

As set forth in relation to the anticipation rejection, the composition produced by the Taketoshi method does not contain ionic bonds. There is no teaching or suggestion in Taketoshi to motivate one of ordinary skill in the art to modify the disclosed composition or method to produce the claimed hybrid wherein interlayer cations in the layered silicates are substituted with hydrogen ions to form ionic bonds between the layered silicates and the drug. Taketoshi does not even recognize the need for any improvement of the disclosed blended composition. Furthermore, Taketoshi fails to provide a reasonable expectation of success that one of ordinary skill in the art can modify the disclosed composition or the disclosed method to produce the claimed hybrid. Therefore, Applicant respectfully submits that no *prima facie* case of obviousness has been established in this rejection.

Moreover, unlike the Office's assertion, the claimed hybrid is unexpectedly superior in stabilizing insoluble drug compound in comparison with the composition produced by Taketoshi. More specifically, the water-soluble organic solvent used in Taketoshi, such as methyl or ethyl alcohol, accelerates the crystallization of the amorphous drug, which results in destabilization of the insoluble drug, as will be shown

in the Declaration. Thus, even if there were *prima facie* case, this unexpectedly superior result would be sufficient to over any *prima facie* case.

For the foregoing reasons, Applicant submits that claims 1-16 would not have been obvious over the Taketoshi and respectfully requests that the rejections under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

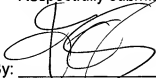
### **CONCLUSION**

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections, and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

  
By: \_\_\_\_\_

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